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10/091,313	03/04/2002	Christine Dingivan	10271-063-999	7146

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EXAMINER	
SKELDING, ZACHARY S	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,313	DINGIVAN, CHRISTINE	
	Examiner	Art Unit	
	Zachary Skelding	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-71* is/are pending in the application.

4a) Of the above claim(s) *2-5, 8-25, 32, 38, 41-61, 64, 65, 67, 68, 70 and 71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,7,26-31,33-37,39,40,62,63,66 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *May 3, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and response of July 11, 2006 has been entered.

   Claims 1-71 are pending.

2. Applicant's election of Group I in the reply filed on July 11, 2006 is acknowledged. ***While Applicant has not formally traversed the restriction requirement***, applicant asserts that examination of all the claimed species could be made without burdening the Examiner; however, applicant has not provided any reasons why examining all species would not impose a serious burden on the examiner.

   Applicant is reminded of the following with respect to the election of species.

   Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.
   Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. See MPEP 809.02(a).

   Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

   Given that applicant has not admitted or provided evidence the species are obvious variants, the species requirement is maintained for the reasons of record, and therefore made **FINAL**.

3. **Claims 1, 6, 7, 26-31, 33-37, 39, 40, 62, 63, 66 and 69 are under examination as they read on** a method of treating an autoimmune disorder or inflammatory disorder comprising administering one or more CD2 binding agents and further comprising an anti-angiogenic factor, wherein the elected species are **"psoriasis"**, **"anti-CD2 antibody"** and **"anti-TNFα antibody"**.

Claims 2-5, 8-25, 32, 38, 41-61, 64, 65, 67, 68, 70 and 71 have been withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being directed to a non-elected invention.

4. The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

5. Applicant is invited to verify the priority date of the instant claims with respect to written support and enablement under 35 USC 112, first paragraph, to the priority documents.

6. Applicant's information disclosure statement, filed May 3, 2005 has been considered.

7. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

   Each letter of trademarked terms should be capitalized wherever it appears and each trademarked term should be accompanied by the generic terminology, e.g., ™ or ®. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

   The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

8. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

9. The specification is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, i.e., "www.pdr.net" in section in section 4.4. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

10. The specification and claims are objected to because the instant specification recites "LFA-3TIP" while claim 30 recites "LFA3TIP", and regardless of which designation is used, consistent terminology should be used throughout the specification and claims.

11. **Claims 1, 7, 30, 33, 40 and 63 are rejected under 35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

    A. Claims 1, 7, 30, 33 and 40, and dependent claims thereof, are indefinite in the recitation of "MEDI-507", "LFA3TIP", "REMICADE" and "ENBREL" as the sole means of identifying these molecules because these terms are merely laboratory designations which do

not clearly define these fusion proteins/antibodies, since different laboratories may use the same designations to define completely distinct biological materials.

Amending the claims to recite the appropriate ATCC Accession Numbers would obviate this rejection.

B. Claim 63 contains the trademark or trade names "REMICADE" and "ENBREL". Where a trademark or trade name is used in a claims as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 USC 112, second paragraph, See Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademarks or the trade names are used to identify or describe "antibodies", and accordingly, the identification or the description is indefinite. The relationship between a trademark or tradename and the product it identifies may be uncertain and arbitrary. The formula or characteristics of the product may change from time to time and yet it may continue to be sold under the same trademark or tradename.

Amending the claims to recite the appropriate ATCC Accession Numbers would obviate this rejection.

C. ***Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.***

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. **Claims 1, 7, 30, 33, 40 and 63, and dependent claims thereof, are rejected under 35 U.S.C. 112, first paragraph,** as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that **"MEDI-507", "LFA3TIP", "REMICADE" and "ENBREL"** fusion protein/antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the pertinent cell lines/hybridomas which produce these fusion protein/antibodies. See 37 CFR 1.801-1.809.

It is noted that LFA3TIP appears to consist of the extracellular domain of LFA-3 fused to the Fc domain of an immunoglobulin molecule. While the instant specification discloses various forms of the extracellular domain of LFA-3 fused to the Fc domain of an immunoglobulin, it does not provide sufficient guidance or direction as to ***which particular form of the extracellular domain of LFA-3*** is fused to the Fc domain of an immunoglobulin in the molecule known as "LFA3TIP". Therefore the instant specification does not put forth sufficient direction or guidance to obtain LFA3TIP by a repeatable method.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit is made after the effective filing date of an application for patent, applicant should promptly submit a verified statement, ***from a person in a position to corroborate the fact***, that the biological material which is deposited is the same as the biological material specifically identified in the application as filed, i.e., is the same as the "MEDI-507", "LFA3TIP", "REMICADE" and "ENBREL" fusion protein/antibodies disclosed in the instant specification. This statement should be verified except if the person is an attorney or agent registered to practice before the Office, in which case the statement need not be verified. See MPEP 1.804(b).

This rejection will be maintained until such time the applicant clarifies for the record the public availability of "MEDI-507", "LFA3TIP", "REMICADE" and "ENBREL" fusion protein/antibodies with respect to the requirements for the deposit of biological materials under 35 U.S.C. § 112, 1st paragraph, see MPEP 2400.

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. **Claims 1, 6, 7, 26-31, 33-37, 39, 40, 62, 63, 66 and 69 are rejected under 35 U.S.C. 103(a)** as being unpatentable over **Bazin et al.** (WO 99/03502) in view of **Wallner et al.** (USSN 6,162,432), **Branco et al.** (Transplantation. 1999 Nov 27;68(10):1588-96)(each of which was cited on applicant's IDS of November 21, 2003), **Le et al.** (USSN 6,277,969) and **Strom et al.** (Therapeutic Immunology edited by Austen et al., Blackwell Science, Cambridge, MA, 1996; see pages 451-456)(see entire documents).

Claims 34 and 37 recite administration of CD2 binding agent at a dose between 0.5-100 μg/kg, which given its broadest reasonable interpretation consistent with the instant specification, encompasses a unit of dose of 0.04–8 mg based on an average weight of 80 kg (176 lbs) for the average human subject having an autoimmune disorder or inflammatory disorder such as psoriasis.

Bazin teaches a method of treating an autoimmune disorder or inflammatory disorder or ameliorating one or more symptoms thereof, said method comprising administering to a subject in need thereof a therapeutically effective amount of one or more CD2 binding molecules, such as an anti-CD2 antibody, for example the monoclonal anti-CD2 antibodies LO-CD2a and MEDI-507, which is humanized LO-CD2a (see entire document, in particular claim 7) Bazin further teaches that the LO-CD2a and MEDI-507 antibodies can be administered at an initial dose of 1 mg via intravenous infusion, and that higher or lower doses may be called for depending upon patient response. Moreover, Bazin teaches that the anti-CD2 antibodies can be combined with other agents that inhibit the activation of T cells, such as other CD2 binding agents (see, in particular page 18, 6th paragraph to page 21, 1st paragraph).

The claimed invention differs from the reference teaching in the recitation of the particular autoimmune/inflammatory disorder "psoriasis", in the recitation of administering of additional biological agents, such as fusion protein that immunospecifically binds CD2, e.g., "LFATIP", and administration of "TNFα antagonists ENBREL and REMICADE".

Wallner teaches a method of treating an autoimmune disorder or inflammatory disorder, such as psoriasis, or ameliorating one or more symptoms thereof, said method comprising administering to a subject in need thereof a therapeutically effective amount of one or more CD2 binding molecules, such as an anti-CD2 antibody including $T11_2$ anti-CD2 antibodies, and/or a fusion protein that immunospecifically binds CD2, such as LFA3TIP (see entire document, in particular the claimed subject matter and columns 1-4, including column 4, lines 44-51). As is well known by one of ordinary skill in the art, $T11_2$ anti-CD2 antibodies are characterized by the fact that they do not inhibit the interaction between CD2 and LFA-3 (see, e.g., Richardson et al., Proc Natl Acad Sci U S A. 1988 Jul;85(14):5176-80, in particular Introduction page 5176).

Wallner further teaches that with regard to administration of a therapeutically effective amount of one or more CD2 binding molecules, such as an anti-CD2 antibody including $T11_2$ anti-CD2 antibodies, and/or a fusion protein that immunospecifically binds CD2, such as LFA3TIP, it will be apparent to those of skill in the art that the effective amount of inhibitor will depend, inter alia, upon the administration schedule, the unit dose administered, whether the inhibitor is administered in combination with other therapeutic agents, the immune status and health of the patient, the therapeutic or prophylactic activity of the particular inhibitor administered and the serum half-life (see, in particular column 16, lines 1-7).

Branco teaches that "MEDI-507 is being investigated for use in autoimmune and other chronic inflammatory conditions such as psoriasis" and that given the biological properties of MEDI-507, it would be desirable to combine administration of MEDI-507 with other biological agents having differing modes of action (see entire document, in particular Introduction and Discussion, pages 1588-1589 and 1594-1595).

Le teaches the administration of anti-TNFα antibody, such as cA2, to treat diseases related to angiogenesis such as psoriasis. Le also teaches that anti-TNFα antibody can be administered in combination with other therapeutic agents (see entire document, in particular columns 34 and 35).

For examination purposes, it is pointed out that the recombinant cA2 anti-TNFα antibody is Remicade.

Strom et al. teach that it was known and practiced by the ordinary artisan to employ a multitiered approach to immunosuppressive therapy similar in principle to that used in chemotherapy, several agents are used simultaneously, each of which is directed to a different molecular targets. Additive-synergistic effects are achieved through application of each agent at relatively low dose, thereby limiting the toxicity of each individual agent while increasing the total immunosuppressive effect (see entire document, including the introduction on page 451).

Given the combined teachings, one of ordinary skill in the art at the time the invention was made would have been motivated and would have had a reasonable expectation of success of treating psoriasis by administering multiple immunosuppressive agents, such as MEDI-507 and/or LFA3TIP, in conjunction with an anti-angiogenesis factor such as the TNFα binding antagonist cA2/REMICADE, as commonly practiced at the time the invention was made, and as taught by the primary and secondary references. Also, it is noted that the teachings of Bazin, Wallner, Branco and Le are consistent with this common practice, as all teach the combination of multiple biological agents to treat an autoimmune/inflammatory disorder, such as psoriasis.

Also, it was prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention.

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. **Claims 6, 7, 26-28, 31, 33-37, 39, 66 and 69 are provisionally rejected** on the ground of nonstatutory obviousness-type double patenting as being unpatentable over ***claims 37-39 and 42-54 of copending USSN 10/091,236.***

The claims of **USSN 10/091,236** recite a method of treating an autoimmune disorder or inflammatory disorder or ameliorating one or more symptoms thereof, said method comprising administering to a subject in need thereof a therapeutically effective amount of one or more integrin $\alpha_v\beta_3$ antagonists and MEDI-507. Given that the instant specification teaches "integrin $\alpha_v\beta_3$ antagonists" are one species of anti-angiogenic agent (see entire document, in particular page 23, 1st paragraph), the claims of the instant application, which recite an "anti-angiogenic agent" are anticipated by the claims of **USSN 10/091,236.**

This is a provisional obviousness-type double patenting rejection.

18. **Claims 6, 7, 26-28, 31, 33-37, 39, 66 and 69** are directed to an invention not patentably distinct from **claims 37-39 and 42-54** of apparently commonly assigned **USSN 10/091,236**. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). The particular commonly assigned claims discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary Skelding whose telephone number is 571-272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding, Ph.D.
Patent Examiner
September 20, 2006

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